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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,732	06/07/2005	Steven W Sutton	JJPR-0177	6621

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
06/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,732	SUTTON ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/29/05, 2/12/07, 5/8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and Claims:

Applicants' election of Invention I (Claims 1-11) without traverse is acknowledged (11 March 2008).

Claims 12-21 are cancelled (11 March 2008).

Claims 1-11 are under examination in the current application.

Claim Rejections

Claim Rejections - 35 USC § 112, first paragraph-Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for the limitations of the claims wherein a method for identifying ligands of the human orexin-2 receptor is performed in cells that non-recombinantly possess the human orexin-2 receptor.

The claims are directed to a method of identifying compounds that modulate the Orexin-2 receptor, by measuring the effects of the candidate compounds on the activity of the orexin-2 receptor, in cells that naturally express the orexin-2 receptor. Dependent claims recite the presence of the receptor in membranes or vesicles, specify certain second messengers, recite use of Ca^{2+} as an indicator, and recite whether the ligand is an agonist, antagonist or inverse agonist. One claim further specifies use of the cells that were assayed in the specification: PFSK-1 cells.

The Orexin-2 receptor binds the large helical peptide hypocretin 2, and probably Orexin-A, NPY and Orexin-B (Lee, et al, 1999, of record; Kane, et al, 2000, of record). It is also believed to be a G-protein-coupled receptor (Kane, et al, 2000). Furthermore, there exist several receptors of this rather large family, found throughout the body, and each with overlapping specificities and selectivities of the hypocretin and orexin ligands (Sakurai, et al, 1998, of record; Kane, et al, 1999; Kirchgessner & Liu, 1999, of record; Lee, 1999, of record).

Applicants have disclosed an assay in which PFSK-1 cells are used for in vitro binding experiments in which orexin B is applied to the cells along with unidentified Ca^{2+} antagonists. Application of the ligand to the cells causes an influx of Ca^{2+} in what can be considered a modified FLIPR assay (See Figure 1 and Example 3).

There are several reasons why enablement of the claimed invention is suspect. The most important consideration is whether specific *Orexin-2* receptors were tested in the assay. First, it is doubtful that the cells themselves have Orexin-2 receptors. PFSK-1 cells are from an immortal cell line derived from a childhood primitive neuroectodermal tumor (Fults, et al, 1992, J. Neuropathol. Exper. Neurol., 51(3): 272-280). There is no evidence that the cells express the adult complement of neuronal receptors or channels, even if their fate as a cell type could have

been determined, which it was not. In fact, the authors state outright that the cells do not express cell-surface antigens (such as membrane receptors) typical of terminally-differentiated neurons (Fults, et al, 1999, abstract). Second, Ca^{2+} flux as a test of receptor activity is a *very* general test. In the patent first describing the assay (Harootunian, et al, 1996, US Patent 5,589,351) the inventors state that FLIPR can be used to measure the activity of most receptors and channels (column 13). Third, as discussed above, orexin and hypocretin receptors are a large family of receptors with overlapping ligand affinities and specificities. It is not clear, therefore, that the Orexin-2 receptor was tested exclusively in the assay, or at all.

Furthermore, the claims are not enabling for use of the human *orexin-2* receptor specifically or exclusively. The claims identify the orexin-2 receptor by name only, rather than SEQ ID NO, and therefore embrace use of variants of the receptor, including non-functioning gene products and allelic variants. The specification provides no guidance on which particular orexin-2 receptor is intended for use in the claimed method.

Similarly, with the exception of claim 4 (which as discussed above, is *not* enabled), the claims embrace use of any cell that expresses a human orexin-2 receptor, without guidance from the specification, or the literature, on which types of cells actually express the receptor.

Due to: 1) the large quantity of experimentation necessary to use a human orexin-2 receptor to identify ligands, 2) the lack of direction/guidance presented in the specification regarding the same, 3) the absence of working examples directed to use of cells comprising the human orexin-2 receptor, 4) the complex nature of the invention, 5) the prior art that contradicts

the idea that PFSK-1 cells comprise orexin-2 receptors, 6) the state of the prior art which is incomplete as far as identification of cells comprising these receptors, as well as which receptors can be considered orexin-2, 7) the unpredictability of relying on a general second-messenger assay to measure the response of a specific receptor, and 8) the breadth of the claims which fail to recite limitations on the orexin-2 receptor used, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention (in its full scope).

Conclusion

No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
28 May 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646